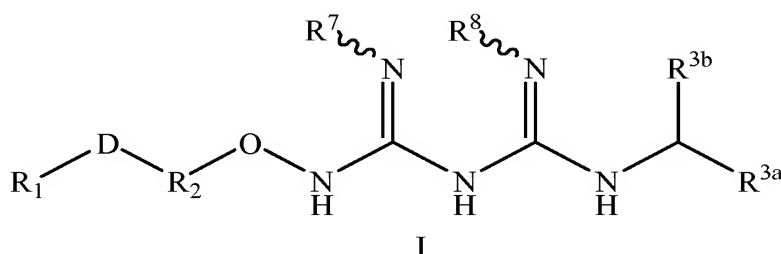


This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

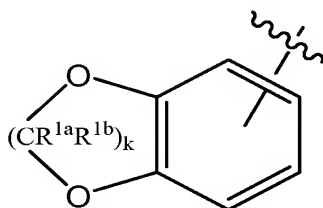
1. *(previously presented)* A compound of formula I or a pharmaceutically acceptable salt thereof:



wherein:

R¹ is R^x, substituted aryl, substituted alkyl, substituted fused cycloalkylaryl, substituted aralkyl, substituted cycloalkylarylalkyl, substituted heteroaryl, or substituted heteroarylalkyl, wherein the latter seven groups are substituted with at least one substituent selected from the group consisting of -CN, -OCF₃, haloalkoxy, -SR⁴, -OCF₃, -SCF₃, haloalkylthio, -NR⁵R⁶, -SO₂R⁴, -SO₂NR⁵R^{6a}, heteroaryl, heterocyclyl or R¹⁰O-(CH₂CH₂O)_j-, or combinations thereof;

R^x is substituted or unsubstituted:



wherein each R^{1a} and R^{1b} are independently H, alkyl or fluoro;

R² is branched or straight chain lower alkylidene, or lower alkylene;

R^{3a} and R^{3b} are each independently hydrogen, lower alkyl, lower alkenyl, lower alkynyl, or taken together form a cycloalkyl group;

each R⁴ is independently hydrogen, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, aryl, substituted aryl, haloaryl, acyl, or heterocyclyl;

each R^5 is independently hydrogen, alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkyl substituted aryl, or acyl;

each R^6 is independently hydrogen, alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkyl substituted aryl, acyl, $-SO_2R^5$, or $SO_2NR^5R^5$; or R^5 and R^6 taken together with the atom to which they are attached form a heterocycle;

each R^{6a} is independently hydrogen, alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkyl substituted aryl, acyl; or R^5 and R^{6a} taken together with the atom to which they are attached form a heterocycle;

R^7 and R^8 are each, independently, hydrogen, alkyl, or acyl;

D is lower alkylidene, lower alkylene, $-O-$, $-S-$, or $-N(R^9)-$;

R^9 is hydrogen, alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkyl-substituted aryl, or acyl;

R^{10} is alkyl or haloalkyl;

j is an integer from 1 to 20; and

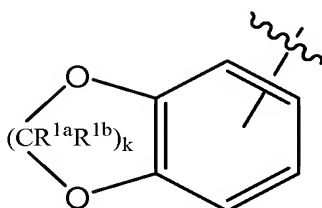
k is an integer from 1 to 4.

2. *(canceled)*

3. *(original)* The compound of claim 1,

wherein R^1 is substituted with at least one substituent selected from the group consisting of $-OCF_3$, haloalkoxy, $-SCF_3$, haloalkylthio or $R^{10}O-(CH_2CH_2O)_j-$.

4. *(original)* The compound of claim 1, wherein R^1 is substituted or unsubstituted:



5. **(original)** The compound of claim 4,
wherein R^x is substituted with one to four substituents selected, independently, from the group consisting of halo, $-\text{NO}_2$, $-\text{CN}$, $-\text{CF}_3$, $-\text{OCF}_3$, haloalkoxy, $-\text{SCF}_3$, haloalkylthio, haloalkyl, lower alkyl, spiroalkyl, aryl, alkoxy, $-\text{SR}^4$, $-\text{NR}^5\text{R}^6$, $-\text{SO}_2\text{R}^4$, $-\text{SO}^2\text{NR}^5\text{R}^{6a}$, heteroaryl, and heterocyclyl, and combinations thereof.
6. **(previously presented)** The compound of claim 1,
wherein when R^1 is substituted aryl, substituted alkyl, substituted fused cycloalkylaryl, substituted aralkyl, substituted cycloalkylarylalkyl, substituted heteroaryl, or substituted heteroarylalkyl, it is further substituted with one to four substituents selected, independently, from the group consisting of halo, $-\text{NO}_2$, $-\text{CF}_3$, haloalkyl, lower alkyl, spiroalkyl, aryl, and alkoxy, and combinations thereof.
7. **(original)** The compound of claim 1,
wherein R^1 is substituted with at least one $-\text{SR}^4$.
8. **(original)** The compound of claim 1,
wherein:
 R^1 is 4-(trifluoromethanethio)-phenyl;
D is $-\text{O}-$; and
 R^7 and R^8 are each hydrogen.
9. **(original)** The compound of claim 1,
wherein R^1 is substituted with at least one $-\text{NR}^5\text{R}^6$.
10. **(original)** The compound of claim 1,
wherein:
 R^1 is 4-(trifluoromethanesulfonamido)-phenyl;
D is $-\text{O}-$; and
 R^7 and R^8 are each hydrogen.

11. **(original)** The compound of claim 1,
wherein R^1 is substituted with at least one $-SO_2R^4$.
12. **(original)** The compound of claim 1,
wherein:
 R^1 is 4-(trifluoromethanesulfonyl)phenyl;
D is -O-; and
 R^7 and R^8 are each hydrogen.
13. **(original)** The compound of claim 1,
wherein:
 R^1 is 2,4-bis-trifluoromethoxyphenyl;
D is -O-; and
 R^7 and R^8 are each hydrogen.
14. **(original)** The compound of claim 1,
wherein:
 R^1 is 4-chloro-3- trifluoromethoxyphenyl;
D is -O-; and
 R^7 and R^8 are each hydrogen.
15. **(original)** The compound of claim 1,
wherein:
 R^1 is 4,5-dichloro-2-trifluoromethoxyphenyl,
D is -O-; and
 R^7 and R^8 are each hydrogen.
16. **(original)** The compound of claim 1,
wherein:
 R^1 is 2-chloro-4-trifluoromethoxyphenyl;

D is -O-; and
R⁷ and R⁸ are each hydrogen.

17. **(original)** The compound of claim 1,
wherein:
R¹ is 4-chloro-2-trifluoromethoxyphenyl;
D is -O-; and
R⁷ and R⁸ are each hydrogen.
18. **(previously presented)** The compound of claim 1,
wherein R^{3a} and R^{3b} are methyl, or taken together form a cyclopropyl group.
19. **(original)** The compound of claim 1,
wherein R¹ is substituted with -CN or -OCF₃.
20. **(original)** The compound of claim 1,
wherein R¹ is substituted with -SCF₃, -SO₂CF₃, or -NHSO₂CF₃.
21. **(previously presented)** The compound of claim 1,
wherein said compound is:
1-(3-(4-trifluoromethoxyphenoxy)propyloxy)-5-isopropyl biguanide;
1-(3-(4-trifluoromethoxyphenoxy)propyloxy)-5-isopropyl biguanide
hemisuccinate;
1-(3-(4-trifluoromethoxyphenoxy)propyloxy)-5-cyclopropyl biguanide;
1-(3-(4-trifluoromethoxyphenoxy)propyloxy)-5-cyclopropyl biguanide
hydrochloride;
1-[3-(2-chloro-4-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide;
1-[3-(2-chloro-4-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide
phosphate salt;
1-[3-(4-chloro-2-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide;

1-[3-(4-chloro-2-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide,
mono phosphate salt;

1-[3-(4-chloro-2-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide,
bis phosphate salt;

1-[3-(2,4-bis(trifluoromethoxy)phenoxy) propyloxy]-5-isopropyl biguanide;

1-[3-(4-chloro-3-trifluoromethoxy phenoxy)propyloxy]-5-isopropyl biguanide;

1-[3-(4,5-dichloro-2-trifluoromethoxy phenoxy)propyloxy]-5-isopropyl
biguanide;

1-[3-(2,2,3,3-Tetrafluoro-2,3-dihydro-benzo[1,4]dioxin-6-yloxy)propyloxy]-5-
isopropyl biguanide;

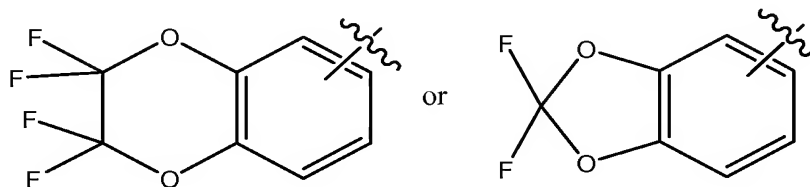
1-[3-(2,2-Difluoro-benzo[1,3]dioxol-5-yloxy) propyloxy]-5-isopropyl
biguanide;

1-[3-(4-(trifluoromethanethio)phenoxy)propyloxy]-5-isopropyl biguanide;

1-[3-(4- (trifluoromethanesulfonamido)phenoxy) propyloxy]-5-isopropyl
biguanide; or

1-[3-(4-(trifluoromethanesulfonyl)phenoxy)propyloxy]-5-isopropyl biguanide.

22. **(original)** A compound of claim 2, wherein when R¹ is R^x, R^x, optionally substituted,
is:



23. **(original)** The compound of claim 6,
wherein R¹ is substituted aryl, substituted cycloalkylaryl, substituted aralkyl,
or substituted cycloalkylarylalkyl.
24. **(original)** The compound of claim 7,
wherein R⁴ of said -SR⁴ is substituted lower alkyl.

25. *(original)* The compound of claim 9,
wherein R⁶ is -SO₂R⁵ or -SO₂NR⁵R^{6a}.
26. *(original)* The compound of claim 11,
wherein R⁴ of said -SO₂R⁴ is substituted lower alkyl.
27. *(previously presented)* The compound of claim 21, wherein said compound is:
1-(3-(4-trifluoromethoxyphenoxy)propyloxy)-5-isopropyl biguanide;
1-(3-(4-trifluoromethoxyphenoxy)propyloxy)-5-isopropyl biguanide
hemisuccinate;
1-(3-(4-trifluoromethoxyphenoxy)propyloxy)-5-cyclopropyl biguanide;
1-(3-(4-trifluoromethoxyphenoxy)propyloxy)-5-cyclopropyl biguanide
hydrochloride;
1-[3-(2-chloro-4-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide;
1-[3-(2-chloro-4-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide
phosphate salt;
1-[3-(4-chloro-2-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide;
1-[3-(4-chloro-2-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide,
mono phosphate salt; or
1-[3-(4-chloro-2-trifluoromethoxyphenoxy)propyloxy]-5-isopropyl biguanide,
bis phosphate salt.
28. *(original)* The compound of claim 22, wherein:
D is -O-; and
R⁷ and R⁸ are each hydrogen.
29. *(previously presented)* The compound of claim 23,
wherein R¹ is mono- or polysubstituted phenyl; and wherein R^{3a} and R^{3b} are
each independently lower alkyl, or taken together form a cycloalkyl group.
30. *(original)* The compound of claim 24,

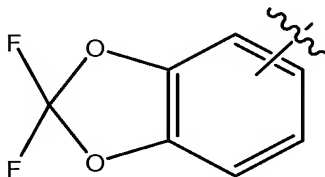
wherein said lower alkyl of R^4 is substituted with at least one halo.

31. *(original)* The compound of claim 25,
wherein R^6 is $-SO_2R^5$.
32. *(original)* The compound of claim 26,
wherein said lower alkyl of said R^4 is substituted with at least one halo.
33. *(previously presented)* The compound of claim 28, wherein:
 R^{3a} and R^{3b} are each methyl, or taken together form a cyclopropyl.
34. *(original)* The compound of claim 29,
wherein:
 R^1 is monosubstituted phenyl.
35. *(original)* The compound of claim 29,
wherein said phenyl is substituted with at least one $-OCF_3$.
36. *(original)* The compound of claim 30,
wherein said halo of R^4 is $-F$.
37. *(original)* The compound of claim 31,
wherein R^5 of said $-SO_2R^5$ is substituted lower alkyl.
38. *(original)* The compound of claim 32,
wherein said halo of said R^4 is $-F$.
39. *(original)* The compound of claim 33, wherein:
 R^2 is $-CH_2CH_2CH_2-$.
40. *(original)* The compound of claim 34,

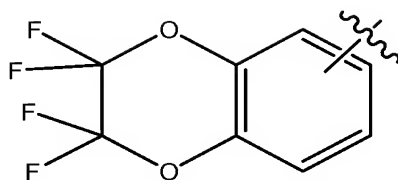
wherein:

R¹ is phenyl substituted with -OCF₃.

41. *(original)* The compound of claim 35,
wherein said phenyl is substituted with at least two -OCF₃.
42. *(original)* The compound of claim 35,
wherein said phenyl, substituted with at least one -OCF₃, is further substituted
with at least one halo.
43. *(original)* The compound of claim 35,
wherein said R^{3a} and said R^{3b} are each methyl.
44. *(original)* The compound of claim 36,
wherein R⁴ is -CF₃.
45. *(original)* The compound of claim 37,
wherein said lower alkyl of R⁵ is substituted with at least one halo.
46. *(original)* The compound of claim 38,
wherein said alkyl of said R⁴ is -CF₃.
47. *(original)* The compound of claim 39, wherein R¹, optionally substituted, is:



48. *(original)* The compound of claim 39, wherein R¹, optionally substituted, is:



49. *(previously presented)* The compound of claim 40,
wherein:
 R^{3a} and R^{3b} are each methyl, or taken together form a cyclopropyl.
50. *(original)* The compound of claim 41,
wherein said phenyl is substituted with two $-OCF_3$.
51. *(previously presented)* The compound of claim 41,
wherein said R^{3a} and said R^{3b} are each methyl, or taken together form a cyclopropyl.
52. *(original)* The compound of claim 42,
wherein said halo of said substituted phenyl is $-Cl$.
53. *(previously presented)* The compound of claim 42,
wherein said R^{3a} and said R^{3b} are each methyl, or taken together form a cyclopropyl.
54. *(original)* The compound of claim 43,
wherein R^2 is $-CH_2CH_2CH_2-$.
55. *(previously presented)* The compound of claim 44,
wherein R^{3a} and R^{3b} are each methyl, or taken together form a cyclopropyl.
56. *(original)* The compound of claim 45,
wherein said halo of R^5 is $-F$.

57. **(previously presented)** The compound of claim 46,
wherein R^{3a} and R^{3b} are each methyl, or taken together form a cyclopropyl.
58. **(original)** The compound of claim 47, wherein R^{3a} and R^{3b} are each methyl.
59. **(original)** The compound of claim 48, wherein R^{3a} and R^{3b} are each methyl.
60. **(original)** The compound of claim 49,
wherein:
 R^1 is *para*-trifluoromethoxyphenyl; and
D is -O-.
61. **(original)** The compound of claim 53,
wherein said R^{3a} and said R^{3b} are each methyl.
62. **(original)** The compound of claim 54,
wherein:
 R^1 is 2,4-bis-trifluoromethoxyphenyl;
D is -O-; and
 R^7 and R^8 are each hydrogen.
63. **(original)** The compound of claim 54,
wherein:
 R^1 is 4-chloro-3- trifluoromethoxyphenyl;
D is -O-; and
 R^7 and R^8 are each hydrogen.
64. **(original)** The compound of claim 54,
wherein:
 R^1 is 4,5-dichloro-2-trifluoromethoxyphenyl;

D is -O-; and
R⁷ and R⁸ are each hydrogen.

65. *(original)* The compound of claim 54,
wherein:
R¹ is 2-chloro-4-trifluoromethoxyphenyl;
D is -O-; and
R⁷ and R⁸ are each hydrogen.

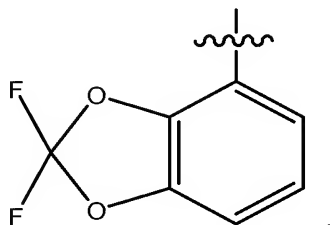
66. *(original)* The compound of claim 54,
wherein:
R¹ is 4-chloro-2-trifluoromethoxyphenyl;
D is -O-; and
R⁷ and R⁸ are each hydrogen.

67. *(original)* The compound of claim 55,
wherein R^{3a} and R^{3b} are each methyl.

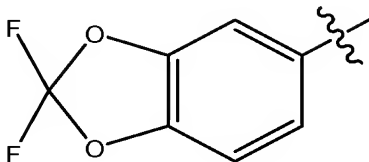
68. *(original)* The compound of claim 56,
wherein said alkyl of R⁵ is -CF₃.

69. *(original)* The compound of claim 57,
wherein R^{3a} and R^{3b} are each methyl.

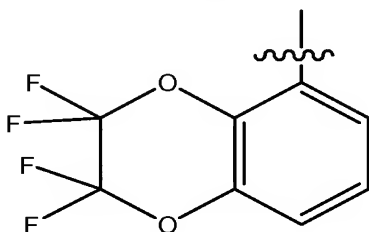
70. *(original)* The compound of claim 58, wherein R¹ is:



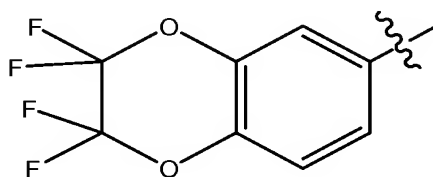
71. **(original)** The compound of claim 58, wherein R¹ is:



72. **(original)** The compound of claim 59, wherein R¹ is:



73. **(original)** The compound of claim 59, wherein R¹ is:



74. **(original)** The compound of claim 60,
wherein:
R⁷ and R⁸ are each hydrogen.

75. **(original)** The compound of claim 61,
wherein said R² is -CH₂CH₂CH₂-.

76. **(original)** The compound of claim 67,
wherein R² is -CH₂CH₂CH₂-.

77. **(previously presented)** The compound of claim 68,
wherein R^{3a} and R^{3b} are each methyl, or taken together form a cyclopropyl.

78. *(original)* The compound of claim 69,
wherein R² is -CH₂CH₂CH₂-.
79. *(original)* The compound of claim 74,
wherein R² is -CH₂CH₂CH₂-.
80. *(original)* The compound of claim 76,
wherein:
R¹ is 4-(trifluoromethanethio)-phenyl;
D is -O-; and
R⁷ and R⁸ are each hydrogen.
81. *(original)* The compound of claim 77,
wherein:
R¹ is 4-(trifluoromethanesulfonyl)phenyl;
D is -O-; and
R⁷ and R⁸ are each hydrogen.
82. *(original)* The compound of claim 78,
wherein R^{3a} and R^{3b} are each methyl.
83. *(original)* The compound of claim 79,
wherein R^{3a} and R^{3b} are each methyl.
84. *(previously presented)* The compound of claim 79,
wherein R^{3a} and R^{3b} taken together form a cyclopropyl.
85. *(original)* The compound of claim 81,
wherein R² is -CH₂CH₂CH₂-.
86. *(original)* The compound of claim 85,

wherein:

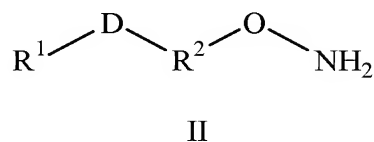
R¹ is 4-(trifluoromethanesulfonamido)-phenyl;

D is -O-; and

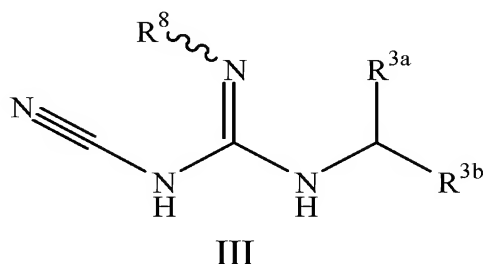
R⁷ and R⁸ are each hydrogen.

87. *(previously presented)* A composition, comprising:
one or more compounds according to claim 1; and
one or more pharmaceutically acceptable carriers.
88. *(previously presented)* The composition of claim 87, further comprising one or more anti-malarial agents or anti-infective agents.
89. *(original)* The composition of claim 87, further comprising at least one sulfonamide or sulfone.
90. *(previously presented)* A process for preparing an antimicrobial compound, comprising the steps of:

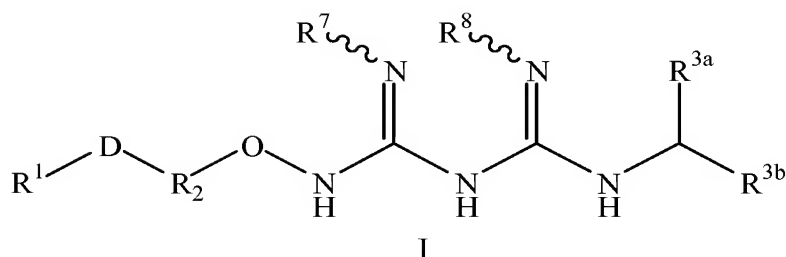
contacting a compound of formula II:



with a compound of formula III:



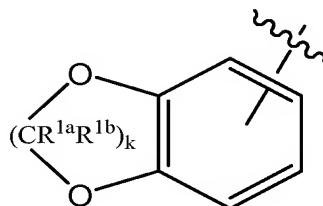
to provide a compound of formula I:



wherein:

R^1 is R^x , substituted aryl, substituted alkyl, substituted fused cycloalkylaryl, substituted aralkyl, substituted cycloalkylarylalkyl, substituted heteroaryl, or substituted heteroarylalkyl, wherein the latter seven groups are substituted with at least one substituent selected from the group consisting of -CN, -OCF₃, haloalkoxy, -SR⁴, -OCF₃, -SCF₃, haloalkylthio, -NR⁵R⁶, -SO₂R⁴, -SO₂NR⁵R^{6a}, heteroaryl, heterocyclyl or R¹⁰O-(CH₂CH₂O)_j-, or combinations thereof;

R^x is substituted or unsubstituted:



wherein each R^{1a} and R^{1b} are independently H, alkyl or fluoro;

R^2 is branched or straight chain lower alkylidene, or lower alkylene;

R^{3a} and R^{3b} are each independently hydrogen, lower alkyl, lower alkenyl, lower alkynyl, or taken together form a cycloalkyl;

each R^4 is independently hydrogen, lower alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, aryl, substituted aryl, haloaryl, acyl, or heterocyclyl;

each R^5 is independently hydrogen, alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkyl substituted aryl, or acyl;

each R^6 is independently hydrogen, alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkyl

substituted aryl, acyl, $-\text{SO}_2\text{R}^5$, or $\text{SO}_2\text{NR}^5\text{R}^5$; or R^5 and R^6 taken together with the atom to which they are attached form a heterocycle;

each R^{6a} is independently hydrogen, alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkyl substituted aryl, acyl; or R^5 and R^{6a} taken together with the atom to which they are attached form a heterocycle;

R^7 and R^8 are each, independently, hydrogen, alkyl, or acyl;

D is lower alkylidene, lower alkylene, $-\text{O}-$, $-\text{S}-$, or $-\text{N}(\text{R}^9)-$;

R^9 is hydrogen, alkyl, substituted lower alkyl, lower alkenyl, substituted lower alkenyl, lower alkynyl, substituted lower alkynyl, alkyl-substituted aryl, or acyl;

R^{10} is alkyl or haloalkyl;

j is an integer from 1 to 20; and

k is an integer from 1 to 4;

or a pharmaceutically acceptable salt thereof.

91-98. *(cancelled)*.

99. *(currently amended)* A method for reducing in a patient the level of infection caused by an organism selected from the group consisting of *Plasmodium sp.*, *Mycobacterium sp.*, *Toxoplasma gondii*, and *Pneumocystis carinii*, comprising the step of:

administering to said patient in need thereof an effective amount of ~~at least~~ one or more compounds according to claim 1.

100. *(currently amended)* A method for protecting a patient susceptible to infection caused by exposure to ~~an organism selected from the group consisting of~~ *Plasmodium sp.*, *Mycobacterium sp.*, *Toxoplasma gondii*, and *Pneumocystis carinii*, comprising the step of:

administering to said patient in need thereof an effective amount of ~~at least~~ one or more compounds according to claim 1.

DOCKET NO.: JACB-0053
Application No.: 10/716,283
Office Action Dated: August 25, 2006

**PATENT
REPLY FILED UNDER EXPEDITED
PROCEDURE PURSUANT TO
37 CFR § 1.116**

101 and 102. *(cancelled)*.